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Review Article

Niosomes A Novel Drug Delivery System

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ABSTRACT

Niosomes are novel multilamellar or unilamellar vesicles, formed by a hydrating mixture of cholesterol and nonionic surfactants.Niosomes are a type of vesicular nanocarrier exploited for enhancing the therapeutic efficacy of various drugs in clinical practice. Niosomes comprise a bilayer hydrophobic membrane enclosing a central cavity filled with an aqueous phase, and therefore, they can encapsulate and deliver both hydrophobic and hydrophilic substances. Niosomal nanocarriers are preferred over other bilayer structures such as liposomes due to their chemical stability, biodegradability, biocompatibility, low production cost, low toxicity, and easy storage and handling. In addition, the niosomal membrane can be easy modified by the inclusion of ligands or stimulus-sensitive segments for achieving targeted delivery and triggered release of the encapsulated cargo. This mini-review outlines the current advances in designing functional niosomes and their use as platforms for developing advanced drug and gene delivery systems.Niosomes remain in the bloodstream for a reasonable time, which is useful for targeted drug delivery. In this chapter, we attempt to introduce these new drug delivery vehicles and give a brief description on the preparation, applications, and advantages and disadvantages of this system. This mini-review outlines the current advances in designing functional niosomes and their use as platforms for developing advanced drug and gene delivery systems.

INTRODUCTION

In the past years, research efforts have been focused on the elaboration of various drug delivery systems, aiming to overcome the limitations of conventional dosage forms and respectively to ensure an improved p bioavailability, reduced side effects, controlled drug release, and targeted delivery. In this context, vesicular systems such as liposomes have successfully been implemented in clinical practice as an advantageous technological approach to achieve the requested demands. The latter boosted the elaboration of different types of vesicular carriers such as niosomes, transferosomes, ethosomes, pharmacosomes, etc.,

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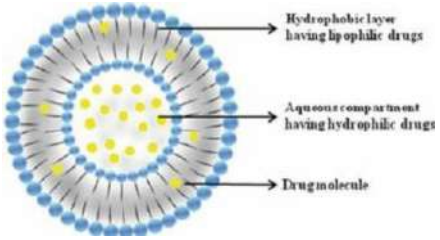
which retain the characteristic lamellar structure, but differ in the type of structural components.Niosomes are a novel drug delivery system, in which the medication is encapsulated in a vesicle. The vesicle is composed of a bilayer of non-ionic surface active agents and hence the name niosomes. Structurally, niosomes are similar to liposomes, in that they are also made up of a bilayer. However, the bilayer in the case of niosomes is made up of non-ionic surface active agents rather than phospholipids as seen in the case of liposomes. Most surface active agents when immersed in water yield micellar structures however some surfactants can yield bilayer vesicles which are niosomes. Niosomes may be unilamellaror multilamellar depending on the method used to prepare them. The niosomes are classified as a function of the number of bilayer (e.g. MLV, SUV) or as a function of size.

Salient features of niosomes.

1. Niosomes can entrap solutes in a manner analogous to liposomes.
2. Niosomes are osmotically active and stable.
3. Niosomes possess an infra structure consisting of hydrophobic and hydrophilic mostly together and so also accommodate the drug molecules with a wide range of solubility.
4. Niosomes exhibits flexibility in their structural characteristics (composition, fluidity and size) and can be designed according to the desired situation.
5. Niosomes can improve the performance of the drug molecules.
6. Better availability to the particular site, just by protecting the drug from biological environment.
7. Niosomes surfactants are biodegradable, biocompatible and non-immunogenic.

Structure of Niosomes.

Structurally, niosomes are similar to liposomes, in that they are also made up of a bilayer. However, the bilayer in the case of niosomes is made up of non-ionic surface active agents rather than phospholipids as seen in the case of liposomes. Most surface active agents when immersed in water yield micellar structures however some surfactants can yield bilayer vesicles which are niosomes. Niosomes may be unilamellaror multilamellar depending on the method used to prepare them.The niosome is made of a surfactant bilayer with its hydrophilic ends exposed on the outside and inside of the vesicle, while the hydrophobic chains face each other within the bilayer. Hence, the vesicle holds hydrophilic drugs within the space enclosed in the vesicle, while hydrophobic drugs are embedded within the bilayer itself. The figure below will give a better idea of what a niosome looks like and where the drug is located within the vesicle. show in figure



Advantages of niosomes.

A. The vesicle suspension is water- based vehicle. This offers high patient compliance in comparison with oily dosage forms.
B. They possess an infrastructure consisting of hydrophilic, amphiphilic and lipophilic moieties together and as a result can accommodate drug molecules with a wide range of solubilities.
C. The characteristics of the vesicle formulation are variable and controllable. Altering vesicle composition, size, lamellarity, tapped volume, surface charge and concentration can control the vesicle characteristics.
D. The vesicles may act as a depot, releasing the drug in a controlled manner.
E. They can reduce drug toxicity because of their non-ionic nature.

Types of niosomes.

The niosomes are classified as a function of the number of bilayer (e.g. MLV, SUV) or as a function of size. (e.g. LUV, SUV) or as a function of the method of preparation (e.g.REV, DRV). The various types of niosomes are described below:

I. Multi lamellar vesicles (MLV),
II. Large unilamellar vesicles (LUV),
III. Small unilamellar vesicles (SUV).

1. Multilamellar Vesicles (MLV):

It consists of a number of bilayer surrounding the aqueous lipid compartment separately. The approximate size of these vesicles is 0.5-10 μm diameter. Multilamellar vesicles are the most widely used niosomes. It is simple to make and are mechanically stable upon storage for long periods. These vesicles are highly suited as drug carrier for lipophilic compounds.

2. Large Unilamellar Vesicles (LUV):

Niosomes of this type have a high aqueous/lipid compartment ratio, so that larger volumes of bio-active materials can be entrapped with a very economical use of membrane lipids.

3. Small Unilamellar Vesicles (SUV):

These small unilamellar vesicles are mostly prepared from multilamellar vesicles by sonication method, French press extrusion electrostatic stabilization is the inclusion of dicetyl phosphate in 5(6)-carboxyfluorescein (CF) loaded Span 60 based niosomes.

Method Of Preparation Of Niosomes.

Niosomes can be prepared by a number of methods which are as follows:

Ether Injection Method

In this method, a solution of the surfactant is made by dissolving it in diethyl ether. This solution is then introduced using an injection (14 gauge needle) into warm water or aqueous media containing the drug maintained at 60°C. Vaporization of the ether leads to the formation of single layered vesicles. The particle size of the niosomes formed depend on the conditions used, and can range anywhere between 50-1000 μm.

Hand Shaking Method (Thin Film Hydration Technique)

In this method a mixture of the vesicle forming agents such as the surfactant and cholesterol are dissolved in a volatile organic solvent such as diethyl ether or chloroform in a round bottom flask. The organic solvent is removed at room temperature using a rotary evaporator, which leaves a thin film of solid mixture deposited on the walls of the flask. This dried surfactant film can then be rehydrated with the aqueous phase, with gentle agitation to yield multilamellar niosomes.

Reverse Phase Evaporation Technique (REV)

This method involves the creation of a solution of cholesterol and surfactant (1:1 ratio) in a mixture of ether and chloroform. An aqueous phase containing the drug to be loaded is added to this, and the resulting two phases are sonicated at 4-5°C. A clear gel is formed which is further sonicated after the addition of phosphate buffered saline (PBS). After this the temperature is raised to 40°C and pressure is reduced to remove the organic phase. This results in a viscous niosome suspension which can be diluted with PBS and heated on a water bath at 60°C for 10 mins to yield niosomes.

Transmembrane pH gradient Drug Uptake Process (Remote Loading)

In this method, a solution of surfactant and cholesterol is made in chloroform. The solvent is then evaporated under reduced pressure to get a thin film on the wall of the round bottom flask, similar to the hand shaking method. This film is then hydrated using citric acid solution by vortex mixing. The resulting multilamellar vesicles are then treated to three freeze thaw cycles and sonicated. To the niosomal suspension, aqueous solution containing 10mg/ml of drug is added and vortexed. The pH of the sample is then raised to 7.0-7.2 using 1M disodium phosphate and mixture

is later heated at 60°C for 10 minutes to give niosomes.

The "Bubble" Method

It is a technique which has only recently been developed and which allows the preparation of niosomes without the use of organic solvents. The bubbling unit consists of a round bottom flask with three necks, and this is positioned in a water bath to control the temperature. Water-cooled reflux and thermometer is positioned in the first and second neck, while the third neck is used to supply nitrogen. Cholesterol and surfactant are dispersed together in a buffer (pH 7.4) at 70°C. This dispersion is mixed for a period of 15 seconds with high shear homogenizer and immediately afterwards, it is bubbled at 70°C using the nitrogen gas to yield niosomes.

Micro Fluidization

Micro fluidization is a recent technique used to prepare unilamellar vesicles of defined size distribution. This method is based on submerged jet principle in which two fluidized streams interact at ultra high velocities, in precisely defined micro channels within the interaction chamber. The impingement of thin liquid sheet along a common front is arranged such that the energy supplied to the system remains within the area of niosomes formation. The result is a greater uniformity, smaller size and better reproducibility of noisome are formed.

Applications Of Niosomes.

The application of niosomal technology is widely varied and can be used to treat a number of diseases.

Niosomes as Drug Carriers

Niosomes have also been used as carriers for iobitridol, a diagnostic agent used for Xray imaging. Topical niosomes may serve as solubilization matrix, as a local depot for sustained release of dermally active compounds, as penetration enhancers, or as rate-limiting membrane barrier for the modulation of systemic absorption of drugs.

Drug Targeting

One of the most useful aspects of niosomes is their ability to target drugs. Niosomes can be used to target drugs to the reticuloendothelial system. The reticulo-endothelial system (RES) preferentially takes up niosome vesicles. The uptake of niosomes is controlled by circulating serum factors called opsonins. These opsonins mark the niosome for clearance. Such localization of drugs is utilized to treat tumors in animals known to metastasize to the liver and spleen. This localization of drugs can also be used for treating parasitic infections of the liver. Niosomes can also be utilized for targeting drugs to organs other than the RES. A carrier system (such as antibodies) can be attached to niosomes (as immunoglobulin's bind readily to the lipid surface of the niosome) to target them to specific organs.

Anti-neoplastic Treatment

Most antineoplastic drugs cause severe side effects. Niosomes can alter the metabolism; prolong circulation and half life of the drug, thus decreasing the side effects of the drugs. Niosomes, is decreased rate of proliferation of tumor and higher plasma levels accompanied by slower elimination.

Leishmaniasis

Leishmaniasis is a disease in which a parasite of the genus Leishmania invades the cells of the liver and spleen. Use of niosomes in tests conducted showed that it was possible to administer higher levels of the drug without the triggering of the side effects, and thus allowed greater efficacy in treatment.

Delivery of Peptide Drugs

Oral peptide drug delivery has long been faced with a challenge of bypassing the enzymes which would breakdown the peptide. Use of niosomes to successfully protect the peptides from gastrointestinal peptide breakdown is being

investigated. In an in vitro study conducted by oral delivery of a vasopressin derivative entrapped in niosomes showed that entrapment of the drug significantly increased the stability of the peptide.

Use in Studying Immune Response

Due to their immunological selectivity, low toxicity and greater stability; niosomes are being used to study the nature of the immune response provoked by antigens. Non-ionic surfactant vesicles have clearly demonstrated their ability to function as adjuvant following parenteral administration with a number of different antigens and peptides.

Niosomes as Carriers for Haemoglobin

Niosomes can be used as carriers for haemoglobin within the blood. The niosomal vesicle is permeable to oxygen and hence can act as a carrier for haemoglobin in anaemic patients.

CONCLUSION:

Niosomes present a structure similar to liposome and hence they can represent alternative vesicular systems with respect to liposomes, due to the niosome ability to encapsulate different type of drugs within their multienvironmental structure. The technology utilized in niosomes is still greatly in its infancy, and already it is showing promise in the fields of cancer and infectious disease treatments. The system is already in use for various cosmetic products. Niosomes represent a promising drug delivery technology various type of drug deliveries can be possible using niosomes like targeting, ophthalmic, topical, parenteral, etc.

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